REMARKS/ARGUMENTS

This is a response to the Office Action dated September 10, 2004. In view of the following remarks and amendments, Applicants respectfully submit that all pending claims are now in condition for allowance.

Claims 1, 3, 16 – 24 and 28 are currently pending in the present application. Claims 2 and 8-15 and 26 have been withdrawn from consideration and Claims 4-7 have been cancelled. Claim 1, 3, 18, 22 are independent claims. By this amendment Claims 1, 3 ,16-19, 22-23 and 28 have been amended and Claims 25 and 27 are canceled.

1. 35 U.S.C. §102(b) rejection based on Logan , et al

Claims 1, 3, 16, 18, 22, 27-28 are rejected under 35 U.S.C. §102(b) as being anticipated by Logan et al (1989) for reasons of record. The Applicant claims the polynucleotide sequence and amino acid sequence consisting of the nucleotide sequence and amino acid sequences as in SEQ ID No. 1 and SEQ ID No. 2, respectively. The Examiner argues that since the language "consisting essentially of" is included in the Claims, Logan teaches the sequence of the Campylobacter flagellin gene and teaches how to make a bivalent, attenuated bacterial expression system (Material and Methods section pages 3031 – 3032) that comprises a plasmid that encodes *Campylobacter* FlaA polypeptide, the polypeptide being encoded by a polynucleotide that comprises the recited range of nucleotides of SEQ ID No. 1.

Response

Anticipation of a claim by a prior art reference can only exist if each and every element is described in a single prior art reference. If a claim is narrowly limited,

anticipation is avoided if the claimed sequences differs from that found in the prior art. *Verdegaal Brox. V. Union Oil Co of California* 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); *Scripps Clinic & Researech Foundation v. Gentech, Inc.,* 927 F.2d 1565, 18 USPQ2d 1001 (Fed. Cir. 1991); *Ex parte Goeddel,* 5 USPQ2d 1449, 1451 (Bd. Pat. App. & Interf. 1987).

The regions of the flagellin gene were specifically selected based on the conserved nature of the DNA sequence among strains. Despite, the use of the truncated, central region, the recombinant protein was found to offer impressive efficacy against Campylabacter challenge in mice. Therefore, Claims 1, 3, 18, and 22 have been amended by deleting "essentially" to reflect the precise sequence encoded by SEQ ID No. 1 and SEQ ID No. 2 to include closed language verses partially open language. The Applicants, therefore, request the rejection be reconsidered and withdrawn.

2. Rejection under 35 U.S.C. §101

Claims 27 and 28, which provide for the use of a polynucleotide sequence, were rejected under 35 U.S.C. §101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process.

Response

Claim 27 has been canceled. Claim 28 has been amended to remove the recitation of a use. Claim 28 is also amended to be dependent on Claim 18 rather than Claim 3. Claim 28, therefore, further limits Claim 18 by adding the limitation of a capability to reduce colonization when said polypeptide is administered as a vaccine.

Applicants, therefore respectfully request the rejection under 35 U.S.C. §101 be reconsidered and withdrawn.

3. Claim Objections

Claims 16-17, 19 and 23 are objected to under 37 CFR §1.75(c), as being improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 16-17, 19 are objected to under 37 CFR §1.75(c)

Examiner states that, in light of the claimed composition of Claim 16 being defined as a polynucleotide in an expression vector, this is not the subject matter of Claim 1 or Claim 18 (isolated and purified). Examiner states that in light of Applicant's comments stating that the polynucleotide is expressed in an expression system, defining the claimed composition as a polynucleotide in an expression vector, which is not the composition of Claim 1 or Claim 18, Claims 16, 17 and 19 are not further limiting of Claim 1 or 18, respectively.

Response

Applicant has amended Claims 16 such that the subject matter is a recombinant expression vector system. Claim 17, as amended, further limits Claim 16 subject matter by requiring an E. coli maltose binding protein gene fused to the said polynucleotide sequence of Claim 16.

Claim 16 is further amended to remove reference to "E. coli" expression vectors since this element is embodied in the reference to "plasmid" expression vectors in Claim

16. As amended, Claims 16 and 17 are fully supported in the specification. No new matter is added.

The Applicants thank the Examiner for the helpful suggestions. Applicants respectfully request that the objections to Claims 16 and 17 under 37 CFR §1.75 (c) be reconsidered and withdrawn.

Claim 19 is objected to under 37 CFR §1.75(c)

Examiner states that, in light of the claimed composition of Claim 16 being defined as a polynucleotide in an expression vector, this is not the subject matter of Claim 1 or Claim 18 (isolated and purified). Examiner states that in light of Applicant's comments stating that the polynucleotide is expressed in an expression system, defining the claimed composition as a polynucleotide in an expression vector, which is not the composition of Claim 1 or Claim 18, Claims 16, 17 and 19 are not further limiting of Claim 1 or 18, respectively.

Response

Dependent claims are permissible if they further limit the claims from which they depend. Claim 16 limits the polypeptide by being "expressed in an expression system.". However, Claim 18, which also contains the element of a polypeptide, does not contain the limitation of "expressed in an expression system." The subject matter of dependent Claim 19 and Claim 18 from which it depends, unlike Claim 16, is an "immunogenic composition." Claim 19 further limits "an immunogenic composition" of Claim 18 by adding the additional element of an E. coli gene encoding maltose binding protein which is fused to the polynucleotide. There is no limitation that the polynucleotide be

expressed. Since Claim 19 further limits its preceeding claim, Claim 19 is a proper dependent claim.

Notwithstanding the above, Claim 18 is amended to better interconnect the elements in order to better define the subject of the claim, an "immunogenic composition." Claim 19 is also amended to better interconnect the elements of this claim, as well. As amended, Claim 18 describes an immunogenic composition. Claim 19 further limits the subject matter of Claim 18 (an immunogenic composition). Claim 18 is also amended to eliminate "E. coli" expression vectors since this element is embodied in the element "plasmid" expression vectors.

The Applicants thank the Examiner for the helpful suggestions. Applicants respectfully request that the objections to Claims 19 under 37 CFR §1.75 (c) be reconsidered and withdrawn.

Claim 23 objected to under 37 CFR §1.75(c)

Examiner objected to Claim 23 under 37 CFR §1.75 (c) for failing to further limit the claim from which it depends. Examiner states that the phrase "an expression vector" in Claim 23 recites a broader genus of expression vectors than those set forth in Claim 22.

Response

Applicant has amended Claim 23 to include "said expression vector." By this amendment, Claim 23 further limits Claim 22. Applicants thank the Examiner for the helpful suggestion and respectfully request the rejection under 37 CFR §1.75(c) be reconsidered and withdrawn.

4. Claim rejections under 35 U.S.C. §112

Rejection of Claims 18-25, 27-28 under 35 U.S.C. §112 (lack of enablement)

Examiner rejected Claims 18-25, 27-28 under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. The Examiner stated that the immungenic/therapeutic composition of Claims 18, 22, 24 and 27-28 do not define any structural sequences, interactions or interrelationships critical to the induction of an immune response. The Examiner also states that the expression vectors are not self replicationg vectors and would not serve to induce an immune respone to the encoded polypeptides in and of themselves. The polynucleotide would need to be incorporated or introduced into an immunocompetant host cell. E. coli, Salmonella and Shigella can serve as selft replicating expression systems, but the polynucleotide has not been incorporated into the bacterial cells and would therefore not serve to induce an immune response to the encoded FlaA polypeptide that the flaA polynucleotide encodes. The Examiner also states that the specification fails to provide an enabling disclosure for the preparation and use of any compositions, including viral vector compositions comprising nucleic acids encoding antigens because it fails to provide adequate guidance regarding how one would have prepared a nucleic acid which when introduced into a host would induce an immune response against the protein encoded by said nucleic acid.

Response

The test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures coupled with information known in the art without

"undue experimentation." *United States v. Telectronics, Inc.* 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988). Undue experimentation is determined by a number of factors including; quantity of experimentation necessary; nature of invention; relative skill of those in the art; amount of direction or guidance presented; presence or absence of working examples; state of the prior art; unpredicatability of the art; and the breadth of the claims. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). However, when a patent specification contains a teaching of a manner and process of making and using the invention in terms which correspond in scope to those used in defining the claimed subject matter, the specification is presumptively enabling. *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367, 369 (C.C.P.A. 1971).

The Examiner states that the specification fails to provide an enabling disclosure for the preparation and use of compositions comprising nucleic acids. However, the Applicants do not claim the use of their constructs for administration as DNA vaccines. Rather, the Applicants claim a flaA sequence that encodes for an immunogenic polypeptide for use in subunit or whole cell bivalent vaccine systems.

The Examiner states that the immunogenic/therapeutic composition of claims 18, 22, 24 and 27, 28 do not define any structural sequences, interactions or interrelationships critical to the induction of an immune response. Claim 18 has been amended to more effectively interrelate elements comprising the claimed subject matter (immunogenic composition) such that the polynucleotide encoding the flaA gene can be expressed in either *E. coli, Shigella* or *Salmonella*. Enabling support for Claim 18 can be found in the specification giving an example for the expression and purification of the truncated flagellin (example 1, using a MBP-FlaA construct) and for the use of the expressed

produced as an immunogen by administering the expressed product to mice (example 3, 4 and 5). Therefore, there is a presumption of enablement in that one skilled in the art would be able to construct, without undue experimentation, a flaA composition suitable for administration as an immunogen.

Claim 22 has been amended to interrelate elements to define relationships critical for the induction of an immune response. Claim 24 is dependent on Claim 22 and further limits the bivalent composition by defining specific carrier bacterial species. Claims 27 has been canceled. Claim 28 has been amended to delete its dependency from Claim 3 and add dependency from Claim 18. By this amendment, Claim 28 further limits the subject of Claim 18, "immunogenic composition", by defining said polypeptide to be capable of reducing colonization by Campylobacter when administered as a vaccine.

Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

Rejection of Claims 16 under 35 U.S.C. 112, second paragraph

Examiner has rejected Claims 16, 22 and 25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Examiner states that Claim 16 encompasses the claimed isolated and purified polynucleotide that "is expressed" in a viral vector. The Examiner further states that since viral and plasmid vectors are not self-replicating, the polynucleotides would not be expressed in the recited viral vector of Claim 16.

Response

Applicant has amended Claims 16 such that it is an independent claim wherein the subject matter of the claim has been changed to a recombinant expression vector system. Furthermore, Claim 16 is amended to interrelate the elements of the claim such that the polynucleotide of Claim 1 is expressed in a DNA expression vector selected from the group consisting of a plasmid or viral expression vector. Support for Claim 16, as amended, can be found Example 1. Claim 16 is further amended to remove "E. coli" expression vectors since this element is embodied in "plasmid" expression vectors.

Applicants respectfully request the rejection under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

Rejection of Claim 22 and Claim 25 under 35 U.S.C. §112, second paragraph

Examiner has rejected Claim 22 under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner states that the E. coli expression system which is a type of carrier strain, and the bacterial carrier strain that will express the encoding polypeptide differ one from the other.

Response

Applicants amend Claim 22 to delete "and E. coli" from paragraph 2 as an element. E. coli expression vectors are embodied under "plasmid" expression vectors. By this amendment, either viral or plasmid expression vectors can be used to transform bacterial cells to obtain bivalent vaccines. Claim 22 is further amended to more clearly interrelate the elements.

Applicants respectfully request the rejection under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

Rejection of Claim 25, under 35 U.S.C. §112, second paragraph

Examiner rejected Claim 25 under 35 U.S.C. §112, second paragraph as being indefinite. Examiner states that Claim 25 is not clearly or distinctly claimed and are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. Therefore, Claim 25 has been canceled.

5. Rejection under 35 U.S.C. §102(b) based on Dumitru, Ioana (1995, dissertation)

Claims 1, 3, 16, 18, 22, 24, 27-28 are rejected under 35 U.S.C. §102(b) as being anticipated by *Dumitru, Ioana* (1995, dissertation). *Dumitru* teaches a recombinant *Campylobacter* DNA sequence encoding the flaA gene (pGEX-2T), minus 258 bp from the C-terminus and that the construct is able to be used to transform *E. coli* or *Salmonella* attenuated bacterial strains. *Dumitru* also teaches a vector that comprises a polynucleotide that encodes for most of the FlaA protein and additionally teaches the construction of fusion peptides between a desired polypeptide coding sequence and *E. coli* heat labile enterotoxin, and a fusion polynucleotide comprising the sequence of flaA fused to the gene GST.

Response

A prior art reference can anticipate a claim only if the reference describes each and every element. *Verdegaal Brox. V. Union Oil Co of California* 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). If a claim is narrowly limited, anticipation is avoided if the claimed sequence differs from that found in the prior art. *Scripps Clinic &*

Research Foundation v. Genetech, Inc., 927 F.2d 1565, 18 USPQ2d 1001 (Fed. Cir. 1991); Ex parte Goeddel, 5 USPQ2d 1449, 1451 (Bd. Pat. App. & Interf. 1987).

Dumitru teaches the construction of a vector containing most of the flaA gene. However, *Dumitru* fails to teach the precise sequence taught by the instant invention. The Applicant claims the polynucleotide sequence disclosed in SEQ ID No. 1 and polypeptide sequence disclosed in SEQ ID No. 2 which include regions I, II and III (see application, Figure 2). Regions outside of this sequence limit are not claimed. The Applicant's claimed region specifically includes the highly conserved N-terminal region and more variable regions II and III (see Figure 2 of application) of the flaA gene. This region was shown to elicit a significant immune response and afforded protection in animal studies (see Table 3 of Specification). *Dumitru* does not teach these precise regions to be used to encode an immunogenic polypeptide. Therefore, Dumitru does not anticipate each element of the claim. Thus, there is no grounds for a *prima facie* case of anticipation under 35 U.S.C. §102(b) regarding Claims 1 and 3 or for dependent Claims 16, 18, 22 and 24, 27-28.

Applicants respectfully request that the rejection under 35 U.S.C. §102(b) be reconsidered and withdrawn.

Respectfully submitted,

Joseph K. Hemby, Jr.
Reg. No. 42,652
Customer No. 22245

Date: December 7, 2004